



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,525	12/29/2003	Tae-Woong Koo	21058/0206735-US0	9348
75172 Client 21058 c/o DARBY & DARBY P.C. P.O. BOX 770 CHURCH STREET STATION NEW YORK, NY 10008-0770				
EXAMINER				
POHNERT, STEVEN C				
ART UNIT		PAPER NUMBER		
1634				
MAIL DATE		DELIVERY MODE		
03/04/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/748,525

Applicant(s)

KOO ET AL.

Examiner

Steven C. Pohnert

Art Unit

1634

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 6-10, 24, 25 and 28-48 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 6-10, 24, 25 and 28-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/2008 has been entered.

Claim status

The instant office action is directed to the supplemental response received on 12/23/2008.

Claims 1-2, 5-10, 24-25, 28-48 are pending and under consideration.

Claims 39-48 have been added by amendment.

Any rejection not specifically reiterated below has been withdrawn.

The 112-2nd rejection of claims 35 and 36 has been withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112-new Grounds

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-2, 5-10, 24-25, 28-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 24 recite the limitation "the unique signal molecules" in the last line. There is insufficient antecedent basis for this limitation in the claim. It is thus unclear if the unique signal molecules are the nucleotide sequences, the distinguishable signal molecules, the oligonucleotide target, or another limitation that is not specifically set recited in the claim. The instant rejection can easily be overcome by amending the claim to recite, "at least one unique signaling molecule. Claims 2, 5-10, 25, 28-48 are rejected as they depend from claims 1 and 24 and thus have all the limitations of the independent claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2, 5, 7-9, 24-25, 28, 31, 32, and 33, 35, 36, 41, 42, 46, 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Cronin et al (US patent 6,045,996, issued April 4, 2000).

The instant rejection has been maintained but modified in view of the amendment and arguments.

The amended claim 1 is drawn to a population of labeled oligonucleotide probes, each labeled oligonucleotide probe comprising an oligonucleotide with a series of distinguishable single molecules, the number and type of the signal molecules identifying the nucleotide sequence of the probe, wherein the each probe is configured

to bind to an oligonucleotide target and the type of nucleotide at each position in at least one of the labeled oligonucleotide probes is configured to be identified by an intensity of at least one unique signal molecule. Thus the broadest reasonable interpretation of the claim requires two oligonucleotide probes, as two probes of the sequence can broadly be interpreted as a population. The oligonucleotide probes must be associated with a series of distinguishable labels the number and type identify the sequence of the probe, thus two copies of a probe of a known sequence labeled with one or more labels, would allow identification of the sequence of the probe. Further the claim requires the probe binds to an oligonucleotide target. The specification teaches, "A "target" or "analyte" molecule is any molecule that can bind to a labeled probe, including but not limited to nucleic acids, proteins, lipids and polysaccharides. In some aspects of methods, binding of a labeled probe to a target molecule can be used to detect the presence of the target molecule in a sample" (0069). Thus the claim requires an oligonucleotide that can bind to a nucleic acid target. The claim concludes by requiring the type of nucleotide at each position in at least one is configured to be identified by the intensity of at least one of the unique signal molecules. Thus the claim as amended requires two probes of a known sequence (potentially the same sequence) that are labeled, such as the intensity (which could be a presence or absence detection) allows for the identification of the probe.

The amended claim 24 is drawn to a reaction mixture, comprising a target polynucleotide and an isolated population of labeled probes, wherein each labeled probe comprises an oligonucleotide with a series of distinguishable single molecules,

the number and type of the signal molecules identifying the nucleotide sequence of the probe, wherein the each probe is configured to bind to an oligonucleotide target and the type of nucleotide at each position in at least one of the labeled oligonucleotide probes is configured to be identified by an intensity of at least one unique signal molecule.

Thus the broadest reasonable interpretation of the claim requires two oligonucleotide probes, as two probes of the sequence can broadly be interpreted as a population. The oligonucleotide probes must be associated with a series of distinguishable labels the number and type identify the sequence of the probe, thus two copies of a probe of a known sequence labeled with one or more labels, would allow identification of the sequence of the probe. Further the claim requires the probe binds to an oligonucleotide target. The specification teaches, "A "target" or "analyte" molecule is any molecule that can bind to a labeled probe, including but not limited to nucleic acids, proteins, lipids and polysaccharides. In some aspects of methods, binding of a labeled probe to a target molecule can be used to detect the presence of the target molecule in a sample" (0069). Thus the claim requires an oligonucleotide that can bind to a nucleic acid target. The claim concludes by requiring the type of nucleotide at each position in at least one is configured to be identified by the intensity of at least one of the unique signal molecules. Thus the claim as amended requires two probes of a known sequence (potentially the same sequence) that are labeled, such as the intensity (which could be a presence or absence detection) allows for the identification of the probe.

With regards to claim 1, Cronin teaches an array of at least 500 different oligonucleotide features per square centimeter at discrete locations (see column 2, lines

23-27). These 500 oligonucleotides are a population of labeled oligonucleotide probes. Cronin further teaches labeling a target with luminescent dyes including polymethine dyes (see column 6, lines 12-22). Cronin further allowing hybridization and determining the identity of the probes to which they are labeled. The hybridization is labeling a probe. Cronin exemplifies this in the example. Cronin's hybridized array is a population of labeled oligonucleotides, comprising an oligonucleotide associated with the detectably distinguishable signal molecules (each labeled molecule is hybridized to a probe at a discrete location), the type and number of signaling molecules is less than the number of probes. As the nucleic acid sequence and location of the probes of Cronin's array are known, the detection of the label allows identification of the type of nucleotide at each position.

With regards to claim 2, Cronin teaches the target can be labeled at one nucleotide (see column 6 line 12). Cronin thus teaches the label is present once, which is less than 4 times.

The specification does not specifically define a reference signal molecule, but teaches an exemplary list in table 1, page 11.

With regards to claim 5, Cronin teaches fluorescein as a label. This is listed in the specification as an exemplary reference signal molecule. Cronin thus teaches probes labeled with reference intensity molecules.

With regards to claim 7 and 8, Cronin teaches the use of polymethine dyes, fluorescein, rhodamine, and so forth (column 6, lines 20-22). Cronin further teaches the

use of Cy3 and Cy5 (see column 9, line 17). Cronin thus teaches oligonucleotide probes labeled with Raman labels, polymethine dyes and signal molecules from table 1.

With regards to claim 9, Cronin et al teaches the fluorescein, rhodamine, CY3, and Cy5 labels (see column 6, lines 20-22; column 9, line 17). Cronin thus teaches fluorescent dyes.

With regards to claim 24, Cronin teaches an array of at least 500 different oligonucleotide features per square centimeter at discrete locations (see column 2, lines 23-27). These 500 oligonucleotides are a population of labeled oligonucleotide probes. Cronin further teaches labeling a target with luminescent dyes including polymethine dyes (see column 6, lines 12-22). Cronin further teaches allowing hybridization of the capture probe and target nucleotide and determining the identity of the probes to which they are labeled. The hybridization is labeling a probe. Cronin exemplifies this in the example. Cronin's hybridized array is a population of labeled oligonucleotides, comprising an oligonucleotide associated with the detectably distinguishable signal molecules (each labeled molecule is hybridized to a probe at a discrete location), the type and number of signaling molecules is less than the number of probes. As the nucleic acid sequence and location of the probes of Cronin's array are known, the detection of the label allows identification of the type of nucleotide at each position.

With regards to claim 25, Cronin teaches the target can be labeled at one nucleotide (see column 6 line 12). Cronin thus teaches the label is present one, which is less than 4 times.

The specification does not specifically define a reference signal molecule, but teaches an exemplary list in table 1, page 11.

With regards to claim 28, Cronin teaches the fluorescein as a label. This is listed in the specification as an exemplary reference signal molecule. Cronin thus teaches probes labeled with reference intensity molecules.

With regards to claim 31 and 32, Cronin teaches the use of polymethine dyes, fluorescein, rhodamine, and so forth (column 6, lines 20-22). Cronin further teaches the use of Cy3 and Cy5 (see column 9, line 17). Cronin thus teaches oligonucleotide probes labeled with Raman labels, polymethine dyes and signal molecules from table 1.

With regards to claim 33, Cronin et al teaches the fluorescein, rhodamine CY3, and Cy5 labels (see column 6, lines 20-22; column 9, line 17). Cronin thus teaches fluorescent dyes.

With regards to claims 35 and 36, Cronin teaches the array is analyzed by a chip detector that generates a signal proportional to the amount of radiation present (column 8, lines 1-10). Cronin thus teaches the location of a peak in the response spectra indicates the presence of a particular label probe and the intensity is proportional to the number of oligonucleotide probes.

With regards to claims 41 and 46, Cronin teaches the target nucleic acid is labeled with one or more nucleotides and thus the hybridized probe has two or more signal molecules attached by 2 or more linkers (column 6, lines 12-13). Thus as nucleotides are labeled by the use of linkers Cronin teaches the use of two or more linkers to link two or more signal molecules.

With regards to claims 42 and 47, Cronin teaches the target nucleic acid is labeled with one or more nucleotides and thus the hybridized probe has two or more signal molecules attached at two or more positions on the probe (column 6, lines 12-13), as the labeled nucleotides of the target hybridize to different nucleotides of the probe.

Response to arguments

The response asserts that Cronin does not anticipate the instant invention as the response asserts that the probes of Cronin are unlabeled oligonucleotides immobilized on the array surface. This argument has been thoroughly reviewed but is not considered persuasive as the probes hybridized to the labeled targets are labeled as discussed in the body of the rejection.

The response continues by asserting, "Cronin's probes are designed to bind to targets for optimal sensitivity and specificity of the hybridization assay, which is achieved by matching the length of the probe to the length of the target. If there is a length mismatch between the target and the probe, the unbound region could bind to another oligonucleotide sequence with partially complementary sequence, which will reduce the sensitivity and specificity of the hybridization assay. Therefore, the intent of a person carrying out a hybridization assay is to match the length of the target and the probe. The functional result is the reduction of an additional binding after hybridization, and the structural result is a hybridized oligonucleotide complex with minimal (or ideally zero) remaining binding region." It appears that counsel is attempting to define the teachings of Cronin, but the examiner could not find basis for such teachings. Thus this

appears to be arguments of counsel that are not supported by evidence, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Here, the statements regarding the array of Cronin must be supported by evidence, not argument.

This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.

Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:

- (1) prior to a final rejection,
- (2) before appeal in an application not having a final rejection, or
- (3) after final rejection and submitted
 - (i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or

(ii) with a satisfactory showing under 37 CFR 1.116(b) or 37

CFR 1.195, or

(iii) under 37 CFR 1.129(a).

Further the assertion that the probe and target must be of the same length contradicts the teachings of Cronin which states the target is often larger than the probe (column 6, lines 43-45).

The response continues that the claimed probes are made such that the labeled probes can be used to bind unlabeled targets. This argument has been thoroughly reviewed but is not considered persuasive as the claim requires the probes be configured to bind oligonucleotide targets, which the hybridized probes of Cronin do. There is no limitation present in the claim requiring the probes not be hybridized to another oligonucleotide, or requiring the label is part of the probe, but the probe is "associated with" which broadly encompasses hybridization as the instant rejection reflects.

The response continues by asserting that Cronin does not teach identifying the type of nucleotide at each position by intensity of the unique signal molecules. This argument has been thoroughly reviewed but is not considered persuasive as Cronin teaches the arrays are made by spatially addressed synthesis, thus the sequence of the probe is known, thus hybridization with a labeled probe allows for the identification of the nucleotides at each position of the oligonucleotide probes.

6. Claim 1, 2, 5-10, 24, 25, 28-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Han et al (Nature Biotechnology (2001) volume 19, pages 631-635).

The instant rejection has been maintained but modified in view of the amendment and arguments.

The amended claim 1 is drawn to a population of labeled oligonucleotide probes, each labeled oligonucleotide probe comprising an oligonucleotide with a series of distinguishable single molecules, the number and type of the signal molecules identifying the nucleotide sequence of the probe, wherein the each probe is configured to bind to an oligonucleotide target and the type of nucleotide at each position in at least one of the labeled oligonucleotide probes is configured to be identified by an intensity of at least one unique signal molecule. Thus the broadest reasonable interpretation of the claim requires two oligonucleotide probes, as two probes of the sequence can broadly be interpreted as a population. The oligonucleotide probes must be associated with a series of distinguishable labels the number and type identify the sequence of the probe, thus two copies of a probe of a known sequence labeled with one or more labels, would allow identification of the sequence of the probe. Further the claim requires the probe binds to an oligonucleotide target. The specification teaches, "A "target" or "analyte" molecule is any molecule that can bind to a labeled probe, including but not limited to nucleic acids, proteins, lipids and polysaccharides. In some aspects of methods, binding of a labeled probe to a target molecule can be used to detect the presence of the target molecule in a sample" (0069). Thus the claim requires an oligonucleotide that can bind to a nucleic acid target. The claim concludes by requiring the type of

nucleotide at each position in at least one is configured to be identified by the intensity of at least one of the unique signal molecules. Thus the claim as amended requires two probes of a known sequence (potentially the same sequence) that are labeled, such as the intensity (which could be a presence or absence detection) allows for the identification of the probe.

The amended claim 24 is drawn to a reaction mixture, comprising a target polynucleotide and an isolated population of labeled probes, wherein each labeled probe comprises an oligonucleotide with a series of distinguishable single molecules, the number and type of the signal molecules identifying the nucleotide sequence of the probe, wherein the each probe is configured to bind to an oligonucleotide target and the type of nucleotide at each position in at least one of the labeled oligonucleotide probes is configured to be identified by an intensity of at least one unique signal molecule. Thus the broadest reasonable interpretation of the claim requires two oligonucleotide probes, as two probes of the sequence can broadly be interpreted as a population. The oligonucleotide probes must be associated with a series of distinguishable labels the number and type identify the sequence of the probe, thus two copies of a probe of a known sequence labeled with one or more labels, would allow identification of the sequence of the probe. Further the claim requires the probe binds to an oligonucleotide target. The specification teaches, "A "target" or "analyte" molecule is any molecule that can bind to a labeled probe, including but not limited to nucleic acids, proteins, lipids and polysaccharides. In some aspects of methods, binding of a labeled probe to a target molecule can be used to detect the presence of the target molecule in a sample"

(0069). Thus the claim requires an oligonucleotide that can bind to a nucleic acid target. The claim concludes by requiring the type of nucleotide at each position in at least one is configured to be identified by the intensity of at least one of the unique signal molecules. Thus the claim as amended requires two probes of a known sequence (potentially the same sequence) that are labeled, such as the intensity (which could be a presence or absence detection) allows for the identification of the probe.

Han et al teaches a method of using multicolor optical coding for biological assays. Han teaches the use of 6 colors and 10 intensities could code for 1 million nucleic acid sequences (see abstract).

With regards to claim 1, Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence.

With regards to claim 2, Han teaches in figure 5, the use of each label only once.

With regards to claim 5, Han et al teaches each labeled oligonucleotide probe is labeled with F by binding of the target nucleic acid (see figure 5).

With regards to claim 6, Han teaches probes of the same length, namely 14 nucleotides, in figure 5 which are from 10 to 50 nucleotides.

With regards to claim 7 and 8, Han teaches the use of adenine in the probes, represented by an A in the nucleotide sequences (see figure 6 and legend). As claim 8 depends from claim 7, the claims teach that adenine is a Raman label. Thus Han teaches Raman labels and signal molecules from table 1.

With regards to claim 9, Han et al teaches the use of quantum dots (see abstract).

With regards to claim 10, Han teaches the use of quantum dots, which are “zinc sulfide-capped cadmium selenide nanocrystals” (see abstract 2nd line). Han thus teaches the use of nanotags.

With regards to claim 24, Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence. Han further teaches the labeled probes are hybridized to a complementary strand and are thus a reaction mixture.

With regards to claim 25, Han teaches in figure 5, the use of each label only once. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is present once.

With regards to claim 28, Han et al teaches each labeled oligonucleotide probe is labeled with F by binding of the target nucleic acid (see figure 5). Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule has an intensity reference signal.

With regards to claim 29 and 30, Han teaches probes of the same length in figure 5 and are from 10 to 50 nucleotides. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each oligonucleotide is identical in length (claims 29 and 30) and length of 10 to 50 nucleotides.

With regards to claim 31 and 32, Han teaches the use of adenine in the probes, represented by an A in the nucleotide sequences (see figure 6 and legend). As claim 32 depends from claim 31, the claims teach that adenine is a Raman label. Thus Han teaches Raman labels and signal molecules from table 1. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is a Raman label or signal molecule from table 1.

With regards to claim 33, Han et al teaches the use of quantum dots (see abstract). Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is a quantum dot.

With regards to claim 34, Han teaches the use of quantum dots, which are "zinc sulfide-capped cadmium selenide nanocrystals" (see abstract 2nd line). Han thus teaches the use of nanotags.

Claims 35 and 36 require the size of the peak is proportional to the number of the particular labeled oligonucleotide pair. This is being broadly interpreted as the size of the peak is proportional to the number of signal molecules.

With regards to claims 35 and 36, Han teaches the size of the peaks is proportional to the number of the signaling molecules in each bead (see figure 1). Han thus teaches the size of the peaks is proportional to the number of labeled signal molecules.

The specification does not set forth a limiting definition of a subunit. Subunit is thus being given the broadest reasonable interpretation as a probe.

With regards to claims 37 and 38, Han teaches the use of beads of 6 colors and 10 intensities could code for 1 million nucleic acid sequences (see abstract). Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence. Each bead is a signal molecule and thus the bead encodes a subunit of a template polynucleotide.

With regards to claims 39-40 and 44-45, Han teaches the probes are single stranded and not immobilized (see figure 5).

The specification does not set forth a limiting definition of linkers. "Linkers" is being given the broadest reasonable interpretation of molecules that are between the labels and probes.

With regards to claims 41 and 46, Han teaches that biotin was attached to oligonucleotides and was associated with streptavidin coated beads to associate with the labeled beads. Thus Han teaches two or more linkers (biotin and streptavidin) were used to associate two or more signal molecules with the probe.

With regards to claims 42 and 47, Han teaches the probe hybridized to the target in which the probe has quantum dot tagged beads and the target beads are attached to a blue fluorescent dye (see figure 5). Thus Han teaches the labeled oligonucleotide probes comprise two or more labels and the series of detectable labels are divided among two labels and the labels are on different positions on the probe.

Claim 43 and 48 are drawn to wherein the detectably distinguishable signal molecules comprise a number of different signal molecules and the number of signal

molecules is equal to the number of labeled bases. The claim thus does not set forth the number of bases that are labeled or that each base is labeled and thus can broadly be interpreted that one a subset of the bases be labeled. Further the claim does not require that the bases are nucleotide bases and thus other broad interpretation may be encompassed by the claims.

With regards to claims 43 and 48, Han teaches probes 1 and 2 have 3 labels and thus the 3 different signal molecules of probes 1 and 2 label 3 different bases (see figure 5).

Response to arguments

The response asserts on the bottom of page 11, that Han does not anticipate the instant claims as the response asserts Han does not teach identifying the type of nucleotide at each position by the intensity of at least one unique signal molecule. These arguments have been thoroughly reviewed but are not considered persuasive as the teachings of Chen couple a known sequence to a known quantum dot tagged bead. Thus the quantum dot fluorescence intensity signature as taught in Figure 5 of Han identifies the entire sequence and thus the nucleotide sequence of the probe.

The response continues by asserting that the specification illustrates the number of unique signal molecules represent the type of nucleotide at each position. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the number of unique signal molecules represent the type of nucleotide at each position) are not recited in the rejected claim(s). Although the claims are interpreted in light of

the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response continues by asserting that the teachings of Han do not allow the artisan to identify the type of nucleotide at each position by only looking at one unique signal molecule and that Han requires the detection of different colors for the code. Thus argument has been thoroughly reviewed but is not considered persuasive as the claims are drawn to the use of at least one unique signaling molecule and thus the claims encompass the use of more than one unique signaling molecule.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steven C Pohnert/
Examiner, Art Unit 1634

Steven Pohnert